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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,215	10/02/2003	Roland Callens	05129-00072-US	9641

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EXAMINER	
KOSAR, ANDREW D	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,215	CALLENS ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *8,13-22,29 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-12,23-28 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: NOTICE TO COMPLY

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 6, 2007 has been entered.

Response to Amendments/Arguments

Applicant's amendments and arguments filed July 6, 2007 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. Applicant's amendments have overcome the previous rejections of record as the art as combined does not teach the Y moiety as currently claimed.

Claims 8, 13-22, 29 and 33-36 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 13, 2006.

Specification/Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

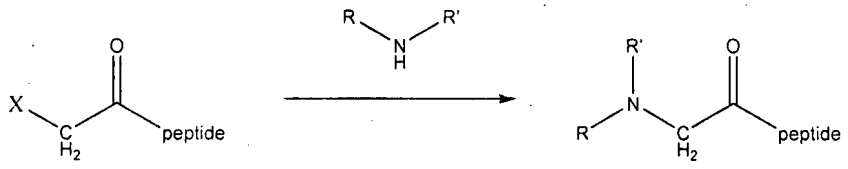
This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, in Applicant's amendments to the specification (see amendment Page 4, amending paragraph beginning at page 10), Applicant has not included a proper sequence identifier for the sequence Gly-Phe-Leu-Gly. It is noted that this sequence is SEQ ID NO:1 in the sequence listing.

Claim Rejections - 35 USC § 103

Claims 1-7, 12, 23-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over SMALES in view of SCHÄFER (PTO-1449, 7/6/07), SAHA and MIMURA.

The instant claims are drawn to a method of making compounds via the general reaction scheme:



, where X is Br or Cl, where the product is the tetrapeptide GFLG and the amine is ammonia.

Smales teaches the peptide GFLG (e.g. Scheme Page 1558).

The difference between Smales and the instant claims is that while Smales teaches the product, Smales does not teach the synthesis as instantly claimed.

The art recognizes reactions of various amines with haloacetylated amino acids, peptides and peptoides to generate N-Gly-peptides (e.g. Canne and Amatsu (EP 0687501A1)) and N^{α}-substituted Gly-peptides (e.g. Marinzi).

Saha teaches synthesis of peptoids, N-substituted polyglycine peptides, using bromoacetylated submonomers in the reaction (e.g. Scheme 2, page 3636). The synthesis is conducted without a resin (solution phase).

Mimura teaches synthesis of chloroacetyltyrosine (Example 1, column 4) and synthesis of GlyTyr via reaction of chloroacetyltyrosine with 28% aqueous ammonia (Example 2, column 5). Mimura teaches that the synthesis of this dipeptide via this mechanism is favored because the product can be formed in "one step in high yields." (column 3, lines 52-53).

Schäfer teaches the synthesis of trishydroxymethylmethane substituted lower peptides from the reaction of R-NH_2 with X-$CH_2C(O)Y$, where R is tris(hydroxymethyl)methane, X is a halogen and Y is an amino acid, di-, tri- or pentapeptide (e.g. claim 1). Schäfer further teaches the synthesis to form Tris-Gly-Gly-Arg-D-Asp-Thr from the reaction of N-2-Br-acetyl-Gly-Arg-D-Asp-Thr reacting with the tris(hydroxymethyl)methane (e.g. Example 3).

It would have been obvious to have made the peptide of Smales, or any other peptide, via reaction of the haloacetylated fragment with ammonia or any substituted amine, in order to form the final product more efficiently with fewer steps and higher yields.

One would have been motivated to have made any peptide, including the peptide GFLG, from the haloacetylated form in order to have an easy and quantitative route for derivitizing peptides and to reduce the number of steps in the process, such as protection/deprotection steps, increase the efficiency of the production and the yield of the product.

One would have had a reasonable expectation for success in forming the product via reaction of the haloacetylated tripeptide with ammonia, as the art recognizes that the reaction of ammonia with haloacetylated amino acids and the reaction of amines with haloacetylated peptides of any size.

Further, with regards to the temperature and concentration ranges, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable

conditions (e.g.temperature ranges, concentration of reactants), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05). One would have been motivated to optimize the conditions in order to achieve the most efficient reaction possible, with a reasonable expectation for success, as they are art recognized variables that are routinely determined and optimized.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1-7, 9-12, 23-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over SMALES in view ofSCHÄFER, SAHA and MIMURA, as applied to claims 1-7, 9, 10, 12, 23-28 and 30-32, *supra*, and in further view of ANTEUNIS (US Patent 4,725,645; PTO-1449, 10/02/03).

The instant claims are presented *supra*, and are further drawn to the method where the

reactant forming products of formula (II) are activated with persilylation.

The teachings of Smales, Schäfer, Saha and Mimura are presented *supra*.

Anteunis teaches using silated amino acids during peptide synthesis, "makes it possible to carry out a rapid coupling reaction in continuous fashion, which reaction takes place without racemisation and can be carried out in the absence of basic coreagents, with water optionally present and in the presence of known protecting agents. In addition, it enables peptides of high molecular weight to be produced in yields higher than those obtained with the known silylating agents. Moreover, the process of the invention enables the water to be chemically consumed and volatile silyl derivatives to be obtained, which facilitates the removal of the later (column 1, line 60 to column 2, line 3).

It would have been obvious to have used silyl activated peptides or amino acids to form the building blocks in order achieve rapid coupling reactions between the subunits.

One would have been motivated to silyl activate the peptides in order to increase the speed and efficiency of the reaction and reduce racemization of the product.

One would have had a reasonable expectation for success in forming the starting material by reaction of silyl activated peptides, as silyl activation and the subsequent use in the synthesis of peptides is a widely practiced technique that can be used to make any peptide.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the

references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andrew D Kosar
Patent Examiner, Art Unit 1654

NOTICE TO COMPLY	Application/Control No.	Applicant(s)	
	10/677,215	CALLENS ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: sequences in the specification do not recite the proper sequence identifier(s).

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
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